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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/510,562	02/22/2000	Gerard Housey	395/35	3061

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EXAMINER
GUZO, DAVID

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/510,562	Applicant(s) HOUSEY, GERARD	
	Examiner David Guzo	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,34,36,37,43-50,59-65 and 71-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,34,36,37,43-50,59-65 and 71-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *21* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 33-4, 36, 43-44, 46, 47, 49, 63, 64, 71-72, 74-75 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Drebin et al.

Applicants and Drebin et al. (Cited by applicants, Cell, Vol. 41, 1985, pp. 695-705, see whole article, particularly the results section on pp. 696-698) both recite a method for inhibiting a particular enzyme (i.e. *neu*-oncogene product) in a cell comprising determining whether a chemical agent (i.e. an antibody) directly interacts with a protein or enzyme whose production in the cell evokes a responsive change (i.e. a graded response) in a phenotypic characteristic of the cell other then the level of the enzyme in the cell by providing a first mammalian cell which overproduces the protein or enzyme and exhibits said phenotypic response to the enzyme and a second mammalian cell which produces the protein or enzyme at a lower level or not at all compared with the first cell line, incubating the chemical agent with both cell lines and comparing the phenotypic response of the cell lines to determine if the agent is an inhibitor of the protein or enzyme and exposing the enzyme in the cell to the agent to inhibit the protein or enzyme. The

antibodies disclosed by Drebin et al. are contemplated for use in contacting cells expressing oncogene products and for use in treating malignancies. Drebin et al. therefore teaches the claimed invention.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 33-34, 36-37, 43-50, 59-65 and 71-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim a method of inhibiting or activating a particular protein or enzyme comprising determining whether a chemical agent that **directly interacts** with the protein or enzyme is an inhibitor or activator of the protein or enzyme and exposing a cell containing the enzyme to the chemical agent so as to inhibit or activate the enzyme.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art

without undue experimentation (See *United States v. Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is needed is not based upon a single factor, but rather is a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) Unpredictability of the art. The art in this area is unpredictable. In order to practice the claimed invention the skilled artisan must be able to distinguish between chemical agents which act **indirectly** to inhibit or activate the target protein or enzyme of interest (POI) vs. those agents which **directly interact** with the POI so as to inhibit or activate the POI. Applicants do indicate that: "Substances which specifically inhibit or inactivate the POI may be distinguished from substances which affect cell morphology or growth by other mechanisms in that they have a greater effect on the test lines than on the control lines." (Specification, p. 5). Applicants also recite: "What we are looking for is a increase in the phenotypic change exhibited by the cell which becomes greater with increased expression of the POI. We call this a "graded response" and it is by this specialized response that we distinguish inhibitors or activators of the POI from agents that act upon other cell metabolites to effect a phenotypic change." (Specification, p. 12). However, this disclosure does not provide guidance on how the skilled artisan would distinguish between chemical agents which directly interact with the POI vs. those which affect the POI by indirect means. For example, if the skilled artisan would attempt to practice the claimed invention to

identify inhibitors or activators of the human bladder c-Ha-ras oncogene (See Hsiao et al., cited by applicants, Mol. Cell. Biol., 1986, Vol. 6, No. 6, pp. 1943-1950) and contacted cells overexpressing the c-Ha-ras oncogene as well as cells which did not express the oncogene, with compounds such as TPA or teleocidin, etc. the skilled artisan would observe a greater phenotypic effect on the test cell line compared with the control line. Given applicants' disclosure, the skilled artisan would identify TPA or teleocidin as a chemical agent which **directly interacts** with c-Ha-ras and serves as an activator of c-Ha-ras. This would not be correct because TPA or teleocidin does not directly interact with c-Ha-ras but instead may function by interacting with cellular protein kinase C receptors or other cellular receptors which in turn may interact in some fashion with the c-Ha-ras oncogene product (p21). Applicants present no teachings on how the skilled artisan would be able to distinguish between false positive results (as discussed above) and results which would emanate from a direct interaction between the POI and chemical agent.

Alternatively, applicants present no disclosure on how the skilled artisan would distinguish between false negative results from true negative results. For example, if the POI was a protein or enzyme in the nucleus and the chemical agent was a compound able to activate or inhibit the POI but was unable to enter the cell or the cell nucleus, or was chemically modified by the cell upon uptake, a false negative result would result. Indeed, the skilled artisan, in order to practice the claimed invention, would have to perform **additional, undisclosed, experimentation** to determine whether the chemical agent initially identified as a inhibitor or activator actually

interacts directly with the POI and serves as an a inhibitor or activator as a consequence of said direct interaction. Given the broad scope of the claims, reading on methods of inhibiting or activating any protein or enzyme expressed in any mammalian cell and given that many POIs of particular interest (i.e. receptors, oncogenes, DNA or RNA binding proteins, etc.) which are involved in cell metabolism or cell growth are components of extremely complex metabolic and physiological pathways and can be influenced by multiple factors which do not directly interact with the POI, it must be considered that the art with regard to methods of inhibiting or activating particular enzymes or proteins in cells is unpredictable.

2) State of the art. The art in the area of developing methods of inhibiting or activating proteins or enzymes (POIs) in cells by chemical agents that directly interact with said POIs and monitoring responsive changes in phenotypic characteristics of the cell evoked by production of the POI is poorly developed.

3) Number of working examples. Applicants present no working examples of the claimed invention wherein a method for inhibiting or activating a particular POI in a cell is accomplished by determining whether a chemical agent that **directly interacts with the POI** is an inhibitor of said POI. Applicants' disclosure provides no mechanism which would enable the skilled artisan to distinguish between chemical agents which interact indirectly with POI and agents which interact directly with the POI.

4) Amount of guidance provided by applicants. As noted above, applicants provide no guidance

on distinguishing a chemical agent which directly interacts with the POI vs. an agent which interacts in some other indirect fashion with the POI. Without such a teaching, the skilled artisan would be unable to practice the instant claims.

5) Scope of the claims. The claims are extremely broad and read on methods of inhibiting or activating any protein or enzyme in a cell.

6) Nature of the invention. The invention involves a complex area in the screening art involving the identification of agents which inhibit or activate proteins or enzymes of interest in cells.

7) Level of skill in the art. The level of skill in the art is high; however, given the lack of guidance provided by applicants, given the unpredictable nature of the art with regard to attempting to identify inhibitors or activators of proteins involved in complex metabolic and biochemical pathways and given the broad scope of the claims, it must be considered that the skilled artisan would have had to have practiced essentially trial and error experimentation in order to attempt to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would need to have conducted undue and excessive experimentation in order to practice the claimed invention.

5. Claims 33-34, 36-37, 43-50, 59-65 and 71-78 are rejected under 35 U.S.C. 112,

first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have not provided a written description of a method of inhibiting or activating a particular POI wherein said method comprises the step of determining whether a chemical agent **that directly interacts with the POI** is an inhibitor or activator of said POI. Applicants have not described a method which is capable of determining whether any given chemical agent directly interacts with the POI and in doing so serves as an inhibitor or activator of the POI. Applicants disclose a method for inhibiting or activating a POI which does not discriminate between chemical agents which directly or indirectly interact with the POI. Successful practicing of the claimed invention would require additional, undisclosed method steps which have not been described.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 33-34, 36-37, 43-50, 59-65 and 71-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33, 43, 59 and 71 (and dependent claims) are vague in that it is unclear if the first and

second mammalian cell lines or the test cell and the control cell are the same cell line, i.e. if the first mammalian cell line is a CHO cell line, does the second cell line also need to be a CHO cell line which produces the POI at a lower level or essentially not at all? If not, it is unclear how the comparisons can be made in a meaningful manner.

Claims 45, 59 and 73 (and dependent claims) are vague in that applicants recite a second or control cell prepared by introducing into a "similar host cell" a second genetic vector "essentially identical" to the first vector except that it does not contain a gene insert. The metes and bounds of the claimed subject matter are vague in that it is unclear how related a "similar" second host cell is to the first host cell. The relationship between the second vector and the first vector is similarly unclear. It is unclear how the term "essentially identical" is to be interpreted, i.e. how closely related can the two vectors be?

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes can be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
November 19, 2001

DAVID GUZO
PRIMARY EXAMINER